

Attorney's Docket 037003-0307368

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re PATENT APPLICATION of:  
NABIL HANNA ET AL.

Confirmation No: 9111

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**DEC 12 2005**

Application No.: 10/743,739

Group Art Unit: 1642

Filed: December 24, 2003

Examiner: Gary B. Nickol

Title: SYNERGISTIC COMPOSITION AND METHODS FOR TREATING  
NEOPLASTIC OR CANCEROUS GROWTHS AND FOR RESTORING OR BOOSTING  
HEMATOPOIESIS

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**CERTIFICATION OF FACSIMILE TRANSMISSION  
UNDER 37 C.F.R. §1.8**

I hereby certify that the following papers, consisting of five sheets  
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Trademark Office at (571) 273-8300 on the date shown below:

Supplemental Information Disclosure Statement

PILLSBURY WINTHROP SHAW PITTMAN LLP



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(Certification of Facsimile Transmission--page 1)

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For: SYNERGISTIC COMPOSITION AND METHODS FOR TREATING NEOPLASTIC OR  
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Sir:

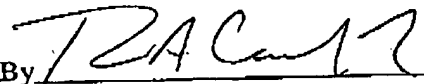
Pursuant to 37 C.F.R. §1.56, 1.97, and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO-1449. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom. Applicants respectfully request the examiner return an initialed copy of the enclosed Form PTO-1449 to applicants with the next Office communication to indicate that the references have been considered, per M.P.E.P. § 609.

The references were cited by the applicant or examiner during the prosecution of U.S. Patent Application No. 09/853,581, filed May 14, 2001, and/or U.S. Patent Application No. 08/933,359, filed on September 18, 1997, to which the present application claims priority pursuant to 35 U.S.C. § 120. Thus, copies of the references listed in the attached PTO-1449 are not attached. This Information Disclosure Statement is being filed before the mailing of a first office action on the merits in the present application. No certification or fee is required.

Respectfully submitted,

Date: December 12, 2005

By



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FORM PTO-1449 (modified)  
To: U.S. Department of Commerce  
(PW FORM PAT-1449)  
Patent and Trademark Office

Atty. Dkt. No.: 037003-0307368

# **SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

Applicant: NABIL HANNA et al.

U.S. Patent Application. No.: 10/743,739

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Date: December 12, 2005

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of

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## **U.S. PATENT DOCUMENTS**

Examiner's Initials	Document Number	Date MM/YYYY	Name (Family Name of First Inventor)	Class	Sub Class	Filing Date (if appropriate)
	AR 2002/0004052 A1	01/2002	Berd et al.	424	277.1	
	BR 5,514,670	05/1996	Friedman et al.	514	2	08/1993
	CR 5,709,860	01/1998	Raychaudhuri et al. (claims only)	---	---	
	DR 5,932,212	09/1999	Khalaf (first page and the page with column 10 only).	---	---	
	ER 6,197,311	03/2001	Raychaudhuri et al. (claims only)	---	---	

## **FOREIGN PATENT DOCUMENTS**

	Document Number	Date MM/YYYY	Country	Inventor Name	English Abstract		Translation Readily Available	
					Yes	No	Enclosed	No
	FR WO 9409815 A1	05/1994	WIPO	Segarini et al.				
	GR							

## **OTHER (Including in this order Author, Title, Periodical Name, Date, Pertinent Pages, etc.)**

HR	Berd et al. "Induction of cell-mediated immunity to autologous melanoma cells and regression of metastases after treatment with a melanoma cell vaccine preceded by cyclophosphamide," Cancer Research, 1986, 46(5):2572-2577.
IR	Blondino et al., "The quantitative determination of aspirin and its degradation products in a model solution aerosol," J Pharm Biomed Anal., 1995, 13(2):111-9 (abstract only).
JR	Brown et al., "Either interleukin-12 or interferon-gamma can correct the dendritic cell defect induced by transforming growth factor beta in patients with myeloma," Br J Haematol. 2004 Jun;125(6):743-8.
KR	Carbone et al., "Class I-Restricted Processing and Presentation of Exogenous Cell-Associated with Antigen In Vivo," February 1990, 171:377-387.
LR	Clarke et al., "Lisofylline inhibits transforming growth factor beta release and enhances trilineage hematopoietic recovery after 5-fluorouracil treatment in mice," Cancer Research, 1996, 56(1):105-112.
MR	Comerci et al., Altered expression of transforming growth factor-beta 1 in cervical neoplasia as an early biomarker in carcinogenesis of the uterine cervix. Cancer. 1996 Mar 15;77(6):1107-14.
NR	Crispens et al., "Evaluation of the anticancer activities of Tweens 20, 40 and 60 in SJL/J mice," Anticancer Res., 1991, 11(1):407-8 (abstract only).
OR	De Wever et al., Critical role of N-cadherin in myofibroblast invasion and migration in vitro stimulated by colon-cancer-cell-derived TGF-beta or wounding. J Cell Sci. 2004 Oct 15;117(Pt 20):4691-4703. Epub 2004 Aug 25.
PR	Dybedal et al., "Transforming growth factor beta (TGF-beta), a potent inhibitor of erythropoiesis: neutralizing TGF-beta antibodies show erythropoietin as a potent stimulator of murine burst-forming unit erythroid colony formation in the absence of a burst-promoting activity," Blood, 1995, 86(3):949-957.
QR	Hasegawa et al., "Transforming growth factor-beta1 level correlates with angiogenesis, tumor progression, and prognosis in patients with nonsmall cell lung carcinoma." Cancer. 2001 Mar 1;91(5):964-71.
RR	Hunter et al., "The Adjuvant Activity of Nonionic Block Polymer Surfactants," J. Immunol., 1981, 127(3):1244-1249.
SR	Jacobsen et al., "Transforming growth factor-beta potently inhibits the viability-promoting activity of stem cell factor and other cytokines and induces apoptosis of primitive murine hematopoietic progenitor cells," Blood 1995, 86(8):2957-2966.
TR	Kopp et al., "Transforming growth factor beta 2 (TGF-beta 2) levels in plasma of patients with metastatic breast cancer treated with tamoxifen," Cancer Research, 1995, 55:4512-4515.

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**SUPPLEMENTAL INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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U.S. Patent Application. No.: 10/743,739

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Examiner: Gary B. Nickol Group Art Unit: 1642

UR	Lee et al., "Aberrant expression of Smad4 results in resistance against the growth-inhibitory effect of transforming growth factor-beta in the SiHa human cervical carcinoma cell line," <i>Int J Cancer</i> . 2001 Nov;94(4):500-7.
VR	Lian et al., "Enhanced expression of transforming growth factor-beta isoforms in the neural tube of embryos derived from diabetic mice exposed to cyclophosphamide," <i>Neurosci Lett</i> . 2003 Nov 6;351(1):51-5.
WR	Matar et al., "Mechanism of antimetastatic immunopotentiality by low-dose cyclophosphamide," <i>Eur. J. Cancer</i> , May 2000, 36(8):1060-1066.
XR	Matar et al., "Down regulation of T-cell-derived IL-10 production by low-dose cyclophosphamide treatment in tumor-bearing rats restores in vitro normal lymphoproliferative response," <i>Int Immunopharmacol</i> . 2001 Feb;1(2):307-19.
YR	Matsunaga et al., "Splenic marginal zone lymphoma presenting as myelofibrosis associated with bone marrow involvement of lymphoma cells which secrete a large amount of TGF-beta," <i>Ann Hematol</i> . 2004 May;83(5):322-5. Epub 2003 Nov 11.
ZR	Medrano et al., "Repression of TGF-beta signaling by the oncogenic protein SKI in human melanomas: consequences for proliferation, survival, and metastasis," <i>Oncogene</i> . 2003 May 19;22(20):3123-9.
AAR	Miller et al., "The Purification and Characterization of the Cytochrome d Terminal Oxidase Complex of the Escherichia coli Aerobic Respiratory Chain," <i>J Biol. Chem.</i> , 1983, 258(15):9159-9165 (page 9159 only).
BBR	Mitani, "Molecular mechanisms of leukemogenesis by AML1/EVI-1," <i>Oncogene</i> . 2004, 23(24):4263-9.
CCR	Mitropoulos et al., "Expression of transforming growth factor beta in renal cell carcinoma and matched non-involved renal tissue," <i>Urol Res</i> . 2004 Sep 7 [Epub ahead of print]
DDR	Moore et al., "Introduction of Soluble Protein into the Class I Pathway of Antigen Processing and Presentation," <i>Cell</i> , September 9, 1988, 54:777-785
EER	Morris et al., "Structural properties of polyethylene glycol-polysorbate 80 mixture, a solid dispersion vehicle," 1992, <i>J Pharm Sci</i> . 81(12):1185-8 (abstract only).
FFR	Piestrzeniewicz-Ulanska et al., "Expression and intracellular localization of Smad proteins in human endometrial cancer," <i>Oncol Rep</i> . 2003 Sep-Oct;10(5):1539-44.
GGR	Sacco et al., "Transforming growth factor beta1 and soluble Fas serum levels in hepatocellular carcinoma," <i>Cytokine</i> . 2000 Jun;12(6):811-4.
HHR	Sansilvestri, "Early CD34high cells can be separated into KIThigh cells in which transforming growth factor-beta (TGF-beta) downmodulates c-kit and KITlow cells in which anti-TGF-beta upmodulates c-kit," <i>Blood</i> , 1995, 86(5):1729-1735.
IIR	Schiemann et al. "Transforming growth factor-beta (TGF-beta)-resistant B cells from chronic lymphocytic leukemia patients contain recurrent mutations in the signal sequence of the type I TGF-beta receptor," <i>Cancer Detect Prev</i> . 2004;28(1):57-64.
JJR	Schmolka, "A Review of Block Copolymer Surfactants," <i>J. Am. Oil. Chem. Soc.</i> , 1977, 54(3):110-116.
KKR	Seoane et al., "Integration of Smad and forkhead pathways in the control of neuroepithelial and glioblastoma cell proliferation," <i>Cell</i> . 2004 Apr 16;117(2):211-23.
LLR	Shariat et al., "Preoperative plasma levels of transforming growth factor beta(1) (TGF-beta(1)) strongly predict progression in patients undergoing radical prostatectomy," <i>J Clin Oncol</i> . 2001 Jun 1;19(11):2856-64.
MMR	Shariat et al., "Preoperative plasma levels of transforming growth factor beta(1) strongly predict clinical outcome in patients with bladder carcinoma," <i>Cancer</i> . 2001 Dec 15;92(12):2985-92.
NNR	Sheen-Chen et al., "Serum levels of transforming growth factor beta1 in patients with breast cancer," <i>Arch Surg</i> . 2001 Aug;136(8):937-40.
OOR	Sitnicka et al., "Transforming growth factor beta 1 directly and reversibly inhibits the initial cell divisions of long-term repopulating hematopoietic stem cells," <i>Blood</i> , 1996, 88(1):82-88.

<b>FORM PTO-1449 (modified)</b> To: U.S. Department of Commerce (PW FORM PAT-1449) Patent and Trademark Office  <b>SUPPLEMENTAL INFORMATION DISCLOSURE          STATEMENT BY APPLICANT</b>	Atty. Dkt. No.: 037003-0307368
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Date: December 12, 2005      Page 3 of 3      Examiner: Gary B. Nickol      Group Art Unit: 1642	

	PPR	Subramanian et al., "Targeting endogenous transforming growth factor beta receptor signaling in SMAD4-deficient human pancreatic carcinoma cells inhibits their invasive phenotype1," Cancer Res. 2004 Aug 1;64(15):5200-11.
	QQR	Takahashi et al., "Induction of CD8 <sup>+</sup> Cytotoxic T Cells by Immunization with Purified HIV-1 Envelope Protein in ISCOMs," Nature, April 26, 1990, 344:873-875.
	RRR	Takiguchi et al., "Profile of cytokines produced in tumor tissue after administration of cyclophosphamide in a combination therapy with tumor necrosis factor," Anticancer Res. 2004, 24(3a):1823-8.
	SSR	Weiner et al., "Treatment of multiple sclerosis with cyclophosphamide: critical review of clinical and immunologic effects," Mult Scler. 2002 Apr;8(2):142-54.
	TTR	Xi et al., "Dysregulation of the TGF-beta postreceptor signaling pathway in cell lines derived from primary or metastatic ovarian cancer," J Huazhong Univ Sci Technolog Med Sci. 2004;24(1):62-5.
	UUR	Xiong et al., "Transforming growth factor-beta1 in invasion and metastasis in colorectal cancer. World J Gastroenterol," 2002 Aug;8(4):674-8.
	VVR	Xu et al., "Elevated serum levels of transforming growth factor beta1 in Epstein-Barr virus-associated nasopharyngeal carcinoma patients," Int J Cancer. 1999 Aug 20;84(4):396-9.

Examiner	Date Considered:
<b>*EXAMINER:</b> Initial if citation considered, whether or not citation is in conformance with MPEP § 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.	